Remarks

Claims 9 and 10 remain for consideration in this application, with both claims being in independent format. Claims 1-8 and 11-12 were previously withdrawn.

The Sequence Listing was alleged not to be in compliance with the rules. Applicants have submitted new copies of the sequence listing with this response, together with the statements that the submission includes no new matter and that the sequence listing submitted on CRF is identical to the sequence listing submitted on paper when the application was filed. Accordingly, Applicants assert that this objection has been overcome.

The Drawings of the application were objected to for being in color without the requisite petition and specification description. In response, Applicants submit herewith the petition under 37 C.F.R. 1.84(a)(2), the petition fee under 37 C.F.R. 1.17(h), and copies of the drawings electronically. Three copies of each drawing are not included herewith as this response is being filed electronically. However, if this is not an appropriate way to respond to this objection, Applicants will provide three copies of each drawing in paper format. Additionally, the specification has been amended as required. Accordingly, Applicants respectfully assert that this objection has been overcome.

The Specification was objected to for containing embedded hyperlinks. Applicants have amended the specification such that these hyperlinks are no longer included, although those of skill in the art will be able to find the web locations through the information provided in place of the hyperlinks. Applicants declare that these amendments add no new matter. Accordingly, Applicants assert that this objection has been overcome.

Claims 9 and 10 were rejected for containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor(s) had possession of the claimed invention. Specifically, it was alleged that the application does not disclose a representative number of known repeat sequences. At the outset, Applicants note that the present claims are for methods of developing a hybridization probe, not for the probes themselves. Thus, if those of skill in the art will be able to practice the invention as claimed using the teachings of the specification and ordinary skill in the art, the claims will satisfy the written description requirement. Claim 9 generally claims a method of developing a hybridization probe wherein the nucleotide-by-nucleotide sequence of a target is compared with the sequences of known repeat sequences and developing a probe complementary to a non-repetitive portion of the target. Claim 10 generally claims a method of identifying a single copy sequence interval from a target nucleic acid by comparing the nucleotide-by-nucleotide sequence of the target nucleic acid with the sequences of known repeat sequences and identifying single copy sequences from such a comparison. It is undeniable that those of skill in the art understand what repeat sequences are, and where the most up-to-date listing of repeat sequences could be found. Furthermore, what repeats are used for practicing the present invention is defined in that the repeats must appear 10 or more times in the genome and have at least 50 nucleotides. The mere fact that this may change over time as new repeat sequences are found does not detract from the fact that the present inventors have developed a method that develops probes and identifies sequences useful for probe formation. As a simplification, if an inventor provides a novel method of changing tires, and demonstrates that his method works

through examples, it does not matter if new tires are developed in the future, if the tires are being changed on a Chevy, Buick, or Honda, or if the tires need to be changed in Kansas, Canada, Australia, or even a road that did not exist at the time the invention was made. If the steps of the method can still be applied, it would be unfair to the inventor to say that such new tires or the different locations for changing tires would prevent them from enjoying the full benefit of their contribution to the art. Several cases were cited in the Office Action as supporting this rejection and particular reference was made to the *Rochester* case. With the present invention, one of skill in the art merely needs to consult an updated database that provides repeat sequences. People of skill in the art are familiar with such databases and they are further directed to them from the present specification. Furthermore, Applicants provided over 400 examples of repeat sequences. In contrast, there is no such database in the *Rochester* case and the inventors did not provide a single example of a compound that would work for their claimed method. In fact, no such compound was known or describable by anything other than an intended function.

With particular respect to the rejection, Applicants assert that the known repeat sequences are defined in that they occur at least 10 times in a genome and are at least 50 nucleotides in length. Applicants further assert that those of skill in the art can determine these repeat sequences from available databases containing sequences of particular genomes. It was alleged "[w]hile a repeat sequence may be known to a researcher, the same repeat sequence may not be known to the general public" (page 6 of the Action). MPEP Section 2163 states, "To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention.

See, e.g., *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116. However, a showing of possession alone does not cure the lack of a written description. *Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 323 F.3d 956, 969-70, 63 USPQ2d 1609, 1617 (Fed. Cir. 2002)." Applicants respectfully assert that, as pointed out in the Action, those of skill in the art or "researchers" know the repeat sequences used to practice the invention and know where to locate them. The standard set forth in the MPEP is that of "one reasonably skilled in the art" and therefore, it is not a requirement that the invention be described in a way that the general public know the inventors had possession. Applicants assert that those of skill in the art are aware of how to locate and select repeat sequences used to practice the methods of the present invention. Furthermore, at the time the application was filed, the application provided information to those of skill in the art of where to find databases of these repeat sequences. The specification on page 3, lines 26-30 states, "As can be appreciated, these initial steps require knowledge of the sequences both of the target and genomic repeats, information which is increasingly available owning to the Human Genome Project and related bioinformatic studies. Furthermore, readily available computer software is used to derive the necessary single copy sequences." Applicants have not only disclosed over 428 examples of repeat sequences, which Applicants assert is a sufficient amount for someone of skill in the art to be able to locate such a sequence, Applicants have also directed those of skill in the art where to find future examples of repeat sequences. Applicants have inquired as to what number of disclosed repeat sequences would be sufficient for a representative number and received no guidance. Many factors and

considerations as to how to determine an appropriate number of sequences are mentioned in the Action, however, it is up to the Examiner to determine what is a sufficient representative amount, and thus far, Applicant has received no guidance with which to fulfill this requirement. Applicants are willing to disclose a greater number of repeat sequences with a declaration; however, Applicants have no guidance as to how many need to be disclosed to be considered adequate written description.

It was also alleged, "no repeat sequences have been provided that were obtained from non-human organisms, such as vertebrates, plants, or microorganisms." Applicants assert that the methods of the present invention are directed towards developing single copy hybridization probes using target and repeat sequences of DNA. The source of the DNA does not make the steps of the method any different as DNA is the same chemically throughout all organisms, and the methods work regardless of the source. The representative number of probes disclosed are repeat sequences of DNA, and therefore, are adequate for any organism which has DNA. Applicants assert that those of skill in the art would be able to practice the method of the present invention to create hybridization probes from DNA sequence regardless of its origin. Accordingly, Applicants respectfully request that this portion of the rejection be withdrawn.

It was additionally alleged that the specification does not disclose a clear relationship between the structure and function of known repeat sequences. Applicants assert that the specification, page 3, lines 21-27 state, "Generally speaking, the probes of the invention are designed by comparing the sequence of a target nucleic acid with known repeat sequences in the genome of which the target is a part; with this information it is possible to deduce the single copy sequences within the target (i.e. those sequences

which are essentially free of repeat sequences which, due to the lack of specificity, can mask the hybridization signal of the single copy sequences)." Applicants assert that the specification clearly teaches to those of skill in the art that the boundaries of the repeat sequences are used to determine a single copy sequence within the target. Without the knowledge of the repeat sequences, probes may contain both repetitive and non-repetitive sequences and hybridization to the target sequence could be impaired or prevented due to the unintentional hybridization to the repeat sequences. This was a problem inherent in the prior art that was overcome using the methods of the present invention. Finally, in response to this rejection, Applicants note that the claims are for the methods, not the probes or the repeats. Accordingly, Applicants assert that this rejection has been overcome.

Claims 9 and 10 were rejected under 35 U.S.C.112, second paragraph, for being indefinite for failing to point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, claims 9 and 10 were alleged to be indefinite over the recitation of "known repeat sequence." It was alleged that "[w]hat constitutes a repeat sequence varies over time, such that what repeat sequence is unknown today, may become known tomorrow." Applicants assert that there will always be repeat sequences within the genome of an individual. Those of skill in the art are familiar with databases and other reference materials which are constantly updated so that the most accurate picture of any given genome is accessible. Applicants assert that those of skill in the art would have the requisite knowledge to obtain the most accurate version of the genome and therefore, be acutely aware of where the repetitive sequences lie. It was also alleged that it is unclear as to how the recitation of "computationally" is intended to further limit

the claims since the determining and identifying steps as further defined in the claims do not include the use of a computer or other numerical means." Applicants respectfully assert that the use of the word "computationally" refers to part of the method in which one of skill in the art would use a genome data base to find and compare the appropriate repeat sequences and a target sequence with which to practice the methods of the present invention. Applicants assert that those of skill in the art know what is meant by "determining the sequence of at least one single copy sequence in said target nucleic acid sequence computationally. . ." Accordingly, Applicants assert that this rejection has been overcome.

Claims 9 and 10 were rejected on the ground of nonstatutory obviousness-type double patenting for being unpatentable over claims 1-8 of U.S. patent No. 6,828,097. Applicants will file a terminal disclaimer upon issuance of the application if such a terminal disclaimer is still warranted.

Claims 9 and 10 were rejected under 35 U.S.C. 102(e) for being anticipated by Kazazian (U.S. Patent No. 6,150,160). It was alleged that Kazazian teaches a method of identifying a single copy sequence interval and methods of developing a hybridization probe to a single copy sequence interval. Applicants respectfully assert that Kazazian discloses that an "L1 retrotransposon may be manipulated using recombinant DNA technology to comprise and/or be contiguous with, other DNA elements which render the retrotransposon suitable for insertion. . ." (column 10). The methods of Kazazian are directed towards "an isolated DNAc molecule comprising a promoter P and a L1 cassette sequence comprising a core L1 retrotransposon element" (column 2). Applicants respectfully assert that the methods of the present invention are directed towards a

method of developing a hybridization probe, which is single copy, which hybridizes to a target nucleic acid sequence. The repeat sequences in the present invention are used to determine the single copy sequence for the probe to hybridize to. In Kazazian, as cited, "Southern blot analysis was carried out on the DNAs of 19-25 different individuals using probes flanking each of the newly isolated active L1s" (column 42). Therefore, in Kazazian, the probes created were used to flank the region of interest. In contrast, the probes of the present invention hybridize to the single copy target sequence, not a sequence that flanks the region of interest (i.e. the single copy sequence). There is nothing to indicate that the target sequence discussed in Kazazian is single copy, as in the present invention. Applicants assert that the probes of Kazazian are not created for the same purpose or to serve the same function as the probes of the present invention, and thus, are distinct. Accordingly, Applicants assert that this rejection has been overcome.

Applicants wish to thank the Examiner for conducting an interview regarding this application. In compliance with MPEP 713.04, Applicants incorporate by reference the interview summary provided by the Examiner after the interview and provide the following as further substance of the interview: The focus of the interview was on the written description rejection articulated by the Examiner. Applicants asserted that the method claims of the present application were fully described in the application such that those of skill in the art would be able to make and use the invention to the fullest extent claimed. Furthermore, Applicants asserted that, to those of skill in the art, the specification fully supported the claims being prosecuted in this application. The Examiner disagreed. No agreement was reached as to these issues. The rejection based on Kazazian was also discussed and the arguments herein are consistent with those

provided in the interview and the Interview Summary provided by the Examiner is also illustrative of the discussion regarding Kazazian.

In view of the foregoing, it is respectfully submitted that all rejections have been overcome and that the claims as they now stand are patentable over the art of record and a Notice of Allowance appears to be in order. Any additional fee due in connection with this Response should be applied against our Deposit Account No. 50-1662.

Respectfully Submitted,

POLSINELLI SHALTON
FLANIGAN SUELTHAUS PC

By: /Tracey Truitt/
Tracey S. Truitt, Reg. No. 43,205
700 W. 47th Street, Suite 1000
Kansas City, Missouri 64112
(816) 753-1000 - Telephone
ATTORNEYS FOR APPLICANTS